Licensure of a Meningococcal Conjugate Vaccine for Children Aged 2 Through 10 Years and Updated Booster Dose Guidance for Adolescents and Other Persons at Increased Risk for Meningococcal Disease — Advisory Committee on Immunization Practices (ACIP), 2011

In January 2011, the Food and Drug Administration lowered the approval age range for use of MenACWY-CRM (Menveo, Novartis Vaccines and Diagnostics), a quadrivalent meningococcal conjugate vaccine, to include persons aged 2 through 55 years. One other quadrivalent meningococcal conjugate vaccine, MenACWY-D (Menactra, Sanofi Pasteur), is licensed in the United States for prevention of meningococcal disease caused by serogroups A, C, Y, and W-135 among persons aged 2 through 55 years; MenACWY-D also is licensed as a 2-dose series for children aged 9 through 23 months (*1,2*). The Advisory Committee on Immunization Practices (ACIP) recommends that persons aged 2 through 55 years at increased risk for meningococcal disease and all adolescents aged 11 through 18 years be immunized with meningococcal conjugate vaccine. ACIP further recommended, in January 2011, that all adolescents receive a booster dose of quadrivalent meningococcal conjugate vaccine at age 16 years (*3*). This report summarizes data supporting the extended age indication for MenACWY-CRM and the interchangeability of the two licensed meningococcal conjugate vaccines.

Safety and Immunogenicity in Children Aged 2 Through 10 Years

The safety and immunogenicity of MenACWY-CRM in children aged 2 through 10 years was evaluated in a multicenter, randomized controlled trial (*1*). A human complement serum bactericidal assay (hSBA) was used to measure antibody responses. Following a single MenACWY-CRM dose, seroresponses to group C, Y, and W-135 in children aged 2 through 5 years and 6 through 10 years were noninferior to responses after a single MenACWY-D dose. Seroresponse was defined as the proportion of subjects with a postvaccination hSBA titer ≥8 if the prevaccination (baseline) titer was <4, or at least a fourfold higher hSBA titer than baseline if the prevaccination titer was ≥4. Overall, the percentage of MenACWY-CRM and MenACWY-D participants aged 2 through 10 years with hSBA titers ≥8 was, respectively, 75% and 80% for serogroup A, 72% and 68% for serogroup C, 90% and 79% for serogroup W-135, and 77% and 60% for serogroup Y (*4*). Injection-site reactions within 7 days after vaccination included pain, erythema, and induration, and were common, with pain being most common. The most common systemic adverse effects were headache and irritability. Rates of adverse effects were similar to those seen after vaccination with MenACWY-D. Serious adverse events were reported in <1% of MenACWY-CRM recipients, and none were attributed to the vaccine.

Use of Meningococcal Conjugate Vaccine in Children Aged 2 Through 10 Years

ACIP recommends vaccination with meningococcal conjugate vaccine for children aged 2 through 10 years at increased risk for meningococcal disease (*3*). A 2-dose primary series is recommended for children with terminal complement deficiencies (e.g., C5–C9, properidin, factor H, or factor D deficiencies) or anatomic or functional asplenia (*5,6*). A single primary dose is recommended for children with increased risk for disease because they are travelers to or residents of countries in which meningococcal disease is hyperendemic or epidemic (e.g., the meningitis belt of sub-Saharan Africa) (*3*). Either meningococcal conjugate vaccine can be used in children aged 2 through 10 years and both are preferred over quadrivalent meningococcal polysaccharide vaccine. This recommendation supersedes the previous recommendation that children aged 2 through10 years should receive only MenACWY-D when meningococcal vaccination is indicated (*2*). Children aged 2 through 10 years with no increased risk for meningococcal disease are not recommended to receive any meningococcal vaccine (*6*).

Interchangeability of MenACWY-CRM and MenACWY-D

In January 2011, ACIP recommended a single booster dose of meningococcal conjugate vaccine for adolescents who received a previous dose before age 16 years (*3*). For persons aged 2 through 55 years at increased risk for meningococcal disease (i.e., persons with asplenia or terminal complement deficiencies, or laboratory workers who work with *Neisseria meningitidis*), a booster dose is recommended if they remain at increased risk (*3,7*).

In a postlicensure study, persistence of hSBA antibodies and the safety and immunogenicity of MenACWY-CRM vaccination were evaluated in persons 3 years after they had received a single dose of MenACWY-CRM or MenACWY-D

(Novartis, unpublished data, 2011). The percentage of participants with hSBA titers ≥8 36 months after a single dose of MenACWY-CRM or MenACWY-D at ages 11 through 18 years was similar for all serogroups (Table 1). After revaccination with MenACWY-CRM, ≥99% of persons previously immunized with MenACWY-CRM or MenACWY-D had hSBA titers ≥8 (Table 2). Injection-site reactions reported within 7 days after revaccination among those who had received MenACWY-CRM followed by MenACWY-CRM or MenACWY-D followed by MenACWY-CRM included pain (45% versus 48%), erythema (7% versus 9%), and induration (11% versus 5%). Systemic adverse events reported by the same groups were headache (24% versus 27%), malaise (5% versus 10%), nausea (8% versus 10%), and fever (2% versus none). The solicited adverse event rates reported after revaccination were similar to the rates reported after primary immunization.

TABLE 1. Percentage of persons with human complement serum bactericidal assay (hSBA) titer ≥8, 3 years after vaccination with a single dose of MenACWY-D* or MenACWY-CRM† at age 11–18 years

	MenACWY-$_D$ (n = 202)		MenACWY-$_{CRM}$ (n = 292)	
Serogroup	%	(95% CI)	%	(95% CI)
A	21	(16–28)	28	(23–33)
C	62	(55–69)	64	(58–69)
W-135	71	(65–77)	82	(77–86)
Y	53	(46–60)	65	(60–71)

Abbreviation: CI = confidence interval.
* Menactra, Sanofi Pasteur.
† Menveo, Novartis Vaccines and Diagnostics.

At this time, no data exist on the use of MenACWY-D following primary vaccination with MenACWY-CRM. Health-care providers should use every opportunity to provide the booster dose when indicated, regardless of the vaccine brand used for the previous dose or doses.

References

1. Food and Drug Administration. Product approval information: package insert. Menveo (Meningococcal [Groups A, C, Y, W-135] oligosaccharide diphtheria CRM197 conjugate vaccine). Rockville, MD: US Department of Health and Human Services, Food and Drug Administration; 2011. Available at http://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm201349.pdf. Accessed August 3, 2011.
2. CDC. Licensure of a meningococcal conjugate vaccine (Menveo) and guidance for use—Advisory Committee on Immunization Practices (ACIP), 2010. MMWR 2010;59:273.
3. CDC. Updated recommendations for use of meningococcal conjugate vaccines—Advisory Committee on Immunization Practices (ACIP), 2010. MMWR 2011;60:72–6.
4. Halperin S, Gupta A, Jeanfreau R, et al. Comparison of the safety and immunogenicity of an investigational and a licensed quadrivalent meningococcal conjugate vaccine in children 2–10 years of age. Vaccine 2010;28:7865–72.
5. CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2005;54(No. RR-7).
6. CDC. Report from the Advisory Committee on Immunization Practices (ACIP): decision not to recommend routine vaccination of all children aged 2–10 years with quadrivalent meningococcal conjugate vaccine (MCV4). MMWR 2008;57:462–5.
7. CDC. Updated recommendation from the Advisory Committee on Immunization Practices (ACIP) for revaccination of persons at prolonged increased risk for meningococcal disease. MMWR 2009;58:1042–3.

TABLE 2. Human complement serum bactericidal assay (hSBA) antibody responses after a booster dose MenACWY-CRM* administered 3 years after a single dose of MenACWY-D† or MenACWY-CRM in persons who received the first dose at age 11–18 years

	Proportion hSBA titer ≥8				Geometric mean titer			
	MenACWY-D† » MenACWY-CRM		MenACWY-CRM » MenACWY-CRM		MenACWY-D » MenACWY-CRM		MenACWY-CRM » MenACWY-CRM	
Serogroup	No.	(%)	No.	(%)	Titer	(95% CI)	Titer	(95% CI)
A	70	(100)	71	(100)	493	(366–664)	356	(256–495)
C	70	(100)	71	(100)	626	(435–901)	703	(473–1,044)
W-135	69	(99)	71	(100)	883	(610–1,278)	987	(656–1,485)
Y	70	(99)	71	(100)	459	(313–671)	679	(447–1,033)

Abbreviation: CI = confidence interval.
* Menveo, Novartis Vaccines and Diagnostics.
† Menactra, Sanofi Pasteur.